IN THE UNITED STATES DISTRICT COURT FOR THE
MIDDLE DISTRICT OF TENNESSEE
NASHVILLE DIVISION

RUTH SMITH, Individually and as Widow for the Use and Benefit of Herself and the Next Kin of Richard Smith, Deceased,	)	
Plaintiff,	)	Civil No. 3:05-0444
	)	Judge Aleta A. Trauger
v.	)	(Dist. Of MA No. 1:05-cv-11515PBS)
PFIZER, INC., *et al.*,	)	
Defendants.	)	

MEMORANDUM IN SUPPORT OF
MOTION TO EXCLUDE TESTIMONY OF DR. GREENLAND

In his proposed written expert testimony, Plaintiff's expert Dr. Sander Greenland offers a statistical calculation regarding the alleged risk of gabapentin that even he concedes has no scientific foundation outside the confines of this litigation. Dr. Greenland cannot point to one instance where any scientific paper anywhere in the world has ever performed the kind of calculation he now proposes to proffer to the jury in this case. Nor can he identify a single instance where he ever performed such a calculation in his entire career. Simply put, lacking the necessary data to support Plaintiff's causation theories, Dr. Greenland improperly tries to create his own. However, an expert is not free to manipulate disparate study findings simply to support a partie's litigation theory. He ignores that FDA's own report determined that the odds ratio of gabapentin to placebo for the risk of suicidal behavior and suicidal ideation is not statistically significant. As more fully set forth below, Dr. Greenland's methodology is fundamentally invalid and would never be employed by a statistician or epidemiologist. Dr. Greenland's newly invented "formula" and the "calculations" he offers are unreliable, inadmissible and should be precluded in their entirety.

I. Dr. Greenland Manipulates the Patorno Study Data To Bolster an Unscientific Methodology That He Invented for This Litigation

In paragraph 7 of his supplemental statement, Dr. Greenland accurately cites the Patorno study from the April 14, 2010 issue of the Journal of the American Medical Association, pp. 1401-1409, as reporting that the "rate of suicidal acts among gabapentin users was 1.42 times (42%) higher than that in topirimate users (95% confidence interval 1.11 to 1.80)." Greenland Statement (Dkt. No. 180-11), ¶ 7. Topiramate is another anti-epileptic drug that the authors of that study used for comparison purposes. He then goes on to note that in "the 2008 FDA report, topirimate patients showed 2.53 times the suicidality risk of placebo patients in clinical trials." *Id.* From these two disparate data points, Dr. Greenland abruptly concludes "[t]hus, relative to a placebo, the excess of risk seen for gabapentin relative to topirimate would correspond to 1.42 times 2.53, or a 3.6-fold increase in risk." *Id.* This calculation, presented for the first time in the litigation, and unprecedented in his or any other epidemiologist's professional work, is patently invalid.

Dr. Greenland takes two different measurements or risk from two different studies and multiplies them to come up with an entirely new "result". Dr. Greenland has multiplied (1) the hazard ratio of gabapentin to topirimate from the Patorno non-randomized observational by (2) the odds ratio of topirimate to placebo from a meta-analysis of randomized placebo-controlled clinical trial conducted by the FDA to "calculate" (3) the relative risk of gabapentin to placebo. To produce a plaintiff-friendly conclusion, Dr. Greenland has merged data from two unrelated studies (one of which, Patorno, is merely an exploratory, un-controlled, and non-randomized study) while ignoring accepted scientific methods of calculating statistical risks. While the FDA did not find a statistically significant relationship between gabapentin and suicidality, Dr. Greenland now purports to find one through nothing more than statistical sleight of hand. Dr.

Greenland cannot cherry-pick data and perform whatever calculations he desires to reach a conclusion supportive of Plaintiff's claims. *Cf. Loeffel Steel Prods. v. Delta Brands, Inc.*, 387 F. Supp. 2d 794, 812 (N.D. Ill. 2005) (observing that *Daubert* requires that "care must be taken to be sure that the comparison is one between 'apples and apples' rather than one between 'apples and oranges'") (citations omitted).

There is no dispute that FDA's own meta-analysis of the gabapentin randomized placebo-controlled clinical trial data (which Dr. Greenland relies upon) put gabapentin's odds ratio at 1.57, with a confidence interval that crosses the 1.0 threshold (i.e., not statistically significant and thereby equally explainable by chance alone). And in a prior declaration, dated July 22, 2008, Dr. Greenland recognized the lack of any finding of increased risk in the FDA report, testifying that "an unbiased assessment of the statistical evidence [in the FDA Alert] shows that the totality of data . . . cannot determine where gabapentin falls (on the spectrum ranging from no harm to harm comparable to topirimate and lamotrigine)." *See* Declaration of Sander Greenland, July 22, 2008 (Dkt No. 1367-1, at 7). Dr. Greenland should not be permitted to now invent on the eve of trial a new risk calculation formula to substitute his elevated, hypothetical odds ratio (3.6) for the actual odds ratio (1.57) that FDA found in its meta-analysis. *See In re Baycol Prods. Litig.*, 532 F. Supp. 2d 1029, 1043 (D. Minn. 2007) (excluding expert's "recalculation" of a study about a drug's risk where the expert "made statistical adjustments that resulted in raising the relative risk of" the drug at issue).

Dr. Greenland's unprecedented attempt to measure gabapentin's risk by multiplying these two disparate findings, while ignoring the FDA's meta-analysis, highlights the lack of any reliable scientific evidence showing an association. Indeed, no published paper that Dr. Greenland could identify has ever ventured to multiply a hazard ratio from a self-proclaimed

"exploratory" observational drug-versus-drug comparison (i.e., no randomized untreated controls) by an odds ratio from a drug-versus-placebo randomized, controlled study to produce any scientifically meaningful number. *See id.* at 1046 (stating that "to recalculate a study, based in part on an unreliable methodology, would render the recalculation unreliable"). Nor could Dr. Greenland recall making a similar calculation in any other context in his entire career as an epidemiologist.

Dr. Greenland admitted as much in his deposition:

> Q: Can you cite for me the name of any paper that you have ever published where you have multiplied the hazard ratio from an observational drug versus drug comparison subject via an odds ratio from a placebo study where you calculate the risk of any drugs relative to a placebo?
>
> A: No.
>
> Q: Can you cite me any paper anywhere in the world that has multiplied the hazard ratio of an observational drug versus drug comparison by an odds ratio from a placebo-controlled study to calculate the new estimate of the risk of any drugs relative to placebo?
>
> A: No.
>
> Q: Have you ever performed this type of analysis before you did it in this case?
>
> A: I can't recall.

See Ex. A, May 5, 2010 Deposition of Dr. Sander Greenland at 116:23-117:14.

Dr. Greenland's selective use of his novel and unique formula to "calculate" gabapentin's risk exposes its lack of scientific validity. If used with the Olesen study,[1] the other observational study Dr. Greenland discusses for the first time in his statement in paragraph 7 comparing gabapentin to another reference drug carbamezapine, the same formula would suggest that gabapentin is in fact *protective* of suicide risk. When asked why he did not use the same

[1] (Ex. 5869, Antiepileptic drugs and risk of suicide: a nationwide dtudy, Olesen et al. (2010))

methodology with the Olesen study risk estimate, Dr. Greenland answered "I don't know. I could do that if you want" before conceding it would indicate a protective effect:

> Q: Dr., what you have to do is you have to take the odds ratio of carbamazepine in the FDA meta-analysis and multiply it by 1.27 in the Olesen papers; correct?
>
> A: Yes, I think you're correct.
>
> Q: So if I, in the carbamazepine analysis or carbamazepine data from figure 2, it is a ratio of .65, and multiply is by 1.27 –
>
> A: I get –
>
> Q: -- correct?
>
> A: I get .81.
>
> Q: Get what?
>
> A: I get .81.
>
> Q: So if you take the data from the Olesen paper of a hazard ratio of 1.27 and multiply it by the reference drug carbamazepine and get the odds ratio of the FDA analysis of .65 is actually that gabapentin has an increased risk of suicide versus placebo; correct?
>
> MR. ALTMAN: Objection. Form.
>
> THE WITNESS: Well, it doesn't demonstrate. ***The estimate comes out as .81, which is on the protective side, but the confidence levels would be extremely wide***.

Ex. A, Greenland Depo. at 118:1-4, 119:1-25 (emphasis added).[2]

Rule 702 and *Daubert* bar Dr. Greenland from telling a jury that he has applied his expertise to "calculate" that gabapentin creates a 3.6-fold increase in the risk of suicide over placebo. Simply put, this is litigation-driven science at its worst. The statement of a 3.6-fold increase in risk is not just highly prejudicial to Pfizer; it is completely divorced from any sound,

[2] Interestingly, Dr. Greenland did not provide any confidence intervals for the new gabapentin "calculation" in his direct statement.

acceptable, statistical methodology that Dr. Greenland or any other epidemiologist or biostatistician would ever use in his professional work. Indeed, the purported "increased risk" is nothing more than a statistical trick to indicate an increased risk from Neurontin where none legitimately exists. It is precisely this type of scientifically unsupported testimony that *Daubert* instructs trial courts, as "gatekeepers," to keep away from juries. *See Nelson v. Tenn. Gas Pipeline Co.*, 243 F.3d 244, 253 (6th Cir. 2001). Dr. Greenland's "calculation" is specially prepared for litigation, dressed up to convey scientific certainty, highly prejudicial to the opposing party, and fundamentally inconsistent with (and unrecognizable in) his underlying scientific discipline. *See Johnson v. Manitowoc Boom Trucks, Inc.*, 406 F. Supp. 2d 852, 859 (M.D. Tenn. 2005) (holding that an "important factor" in any *Daubert* analysis "is whether the expert is testifying about matters arising naturally and independently of litigation or whether opinions are developed solely for the purpose of testifying"). Of course, his formula has never been peer-reviewed, tested, or accepted in any scientific community. In other words, it looks like it means something when, in fact, it means nothing.

CONCLUSION

For the reasons set forth above, Dr. Greenland's computation that gabapentin poses a hypothetical 3.6-fold increase in risk is scientifically invalid, unreliable, and misleading, and should properly be precluded from the jury's consideration under Daubert and FRE 702.

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on this the 14th day of May 2010, I electronically filed the foregoing document with the Clerk of the Court, United States District Court for the Middle District of Tennessee, using the CM/ECF system. True and correct copies of the foregoing documents are being served via the Court's CM/ECF system on the following:

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